CANCER

First Combined Analysis from INTERPHONE Inconclusive

Long-awaited results of the largest effort yet to investigate whether cell phone use contributes to brain cancers are finally available.[1] But the May report, the first combined analysis of results from the International Agency for Research on Cancer's (IARC) $24-million INTERPHONE study, is inconclusive, stating that "suggestions of an increased risk of glioma at the highest exposure levels, but biases and errors prevent a causal interpretation."

The interview-based case–control INTERPHONE study was the collaborative effort of 48 researchers from 13 nations. It began in 2000 and included more than 14,000 participants, among them 2,765 glioma and 2,425 meningioma cases and matched controls[2] (the current analysis included 2,708 glioma and 2,409 meningioma cases). No other studies have included as many exposed cases, particularly of long-term and heavy users of cell phones.

A major challenge the researchers faced in interpreting the data was the high refusal rates among controls—that is, controls were successfully contacted but declined to give the information sought—says the study's principal investigator, Elisabeth Cardis, now of the Centre for Research in Environmental Epidemiology in Barcelona, Spain. "This resulted in mobile phone users being overrepresented among controls," Cardis explains. The vast majority of the study's risk estimates are below 1, which suggests there might have been a selection bias in amassing the study population, she says.

Additionally, cell phone usage patterns have changed significantly in the decade since INTERPHONE began. "Most of the users in the study had relatively low use compared to today's use," Cardis points out. The usage by people in the study's highest cumulative call time group corresponds to about half an hour a day for a period of 10 years or more, which is "pretty normal or even light use today," she says. At the same time, concerns over recall bias also made the data hard to interpret. For example, some cases—but no controls—claimed to spend 12 or more hours a day on their cell phone.

In the most recent industry figures from CTIA,[7] U.S. cell phone users logged about 2.3 trillion minutes of use per year, but many users are reporting an increase in text messages over calls.

Besides the brain tumors assessed in the current study, INTERPHONE also evaluated correlations between cell phone use and tumors of the acoustic nerve and the parotid salivary gland. These two tumor types will be the focus of future reports, Cardis says.

The period of exposure for all of the subjects included in INTERPHONE is relatively short for assessing a causative link to a cancer, according to a commentary published alongside the study.[3] Cell phone use began in the 1980s but was not widespread until the mid-1990s, wrote authors Rodolfo Saracci of Italy's National Research Council in Pisa and Jonathan Samet of the University of Southern California's Department of Preventive Medicine. "None of . . . today's established carcinogens, including tobacco, could have been firmly identified as increasing risk in the first 10 years or so since

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The Beat

by Erin E. Dooley

EWG Issues 2010 Sunscreen Guide

In its fourth report on sunscreen products, the Environmental Working Group recommends only 8% of 500 products tested.[1] The group reports a surge in products boasting an SPF higher than 50, "which sell a false sense of security" since higher SPF does not necessarily equate to more protection. Several products contained ingredients of potential health concern: retinyl palmitate, which has been linked to accelerated development of skin tumors and lesions, was found in 41% of sunscreens assessed, and oxybenzone, an endocrine-disrupting compound, was found in 60%.

Contrary to public perception, there is no evidence sunscreen prevents skin cancer.

EPA Exposure Assessment: PBDEs

A new EPA exposure assessment[2] shows that U.S. exposure to polybrominated diphenyl ethers (PBDEs) occurs primarily through house dust, unlike other persistent organic pollutants, which typically are encountered in food. Additionally, weight-specific intake rates are higher for U.S. children, especially infants, than for adults. The EPA is planning to issue new rules later this year for the manufacture and import of products containing two specific PBDEs. PBDE flame retardants, some of which have already been phased out of commerce, are used in applications including furniture and electronics.

"Safer" cigarettes? Nice try, but no cigar.

"Safer" Cigarettes Still Hazardous

Smoking tobacco- and nicotine-free cigarettes made of lettuce may be at least as hazardous as smoking conventional tobacco cigarettes, if not more so. In a study of the supposedly safer cigarettes, which were introduced in 1997, dose-dependent double-strand DNA breaks were seen after shorter durations of exposure to smoke compared with conventional cigarettes.[3]

Left to right: iStockphoto.com; Shutterstock

first exposure," explained Saracci and Samet. "Ionizing radiation is a recognized cause of brain tumors, but except for rare instances the radiation-induced cases occur on average after 10–20 years since the time of first exposure." The authors conclude, therefore, that "observing no increase in risk would be reassuring but only to a limited extent."

Publication of the first results from INTERPHONE was originally expected in 2006. Cardis says the report was delayed because of the large research team's difficulties in interpreting the results. "The entire study group and all of the coauthors . . . spent a lot of time conducting hundreds of additional analyses, reviewing the analyses, and trying to understand the potential biases of the study," she says. "We've conducted about every analysis that we could think to do."

One of the analyses that did not make it into the main text of the report is Appendix 2, which is mentioned in Saracci and Samet's commentary. Published only online as supplementary material, it presents an alternative analysis that suggests an increase in glioma among subjects in the top 10% of cumulative call time. The alternative analysis compared the incidence of glioma in the most highly exposed subjects to that in study subjects who had the lowest amount of exposure among regular cell phone users. In contrast, the primary analysis compared the incidence of glioma in the highly exposed group to the incidence among subjects who reported that they rarely or never used cell phones at all.

This approach—which accounts for the possibility that cell phone radiation exposure is not the only potential risk factor that differs between people who regularly use cell phones and people who don't—is common in occupational epidemiology. However, some INTERPHONE investigators believed the analysis would be inappropriate if the main reason for the decreased odds ratios observed in the study was not selection bias. "We have legitimate differences in the interpretation of these results and the value of this analysis," Cardis says.

IARC director Christopher Wild says, "Observations at the highest level of cumulative call time and the changing patterns of mobile phone use since the period studied by INTERPHONE, particularly in young people, mean that further investigation of mobile phone use and brain cancer risk is merited." John Walls, vice president of public affairs for CTIA-The Wireless Association®, which represents the cell phone industry, says, "The possible effects of long-term heavy use of mobile phones require further investigation."

Three important new studies are already under way to collect more data. The first is an animal study being conducted by the National Toxicology Program to assess the effects of long-term exposure to radiofrequency energy in rats and mice.[4] The study allows for precise control over the exposure, as well as a "thorough evaluation for the presence of tumors, not just of the brain, but throughout the entire body," says program associate director John Bucher.

The other two studies are epidemiologic. The case–control MOBI-KIDS study was launched last year in 13 countries to investigate potential risk factors for brain tumors in children, including cell phone use.[5] Children's rates of brain cancers have been rising in recent years, according to the study's organizers, who hope to recruit approximately 2,000 brain cancer patients and matched controls. The COSMOS cohort study, launched in April with the specific goal of studying health effects of cell phone use, aims to recruit more than 250,000 people in five European countries and follow them for up to 30 years.[6]

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The tobacco- and nicotine-free cigarettes also delivered far higher doses of total particulate matter ("tar").The researchers used phospho-specific antibodies to measure DNA damage response and their own laser scanning cytometry instrumentation, which they say should be a useful complement to other methods for assessing genotoxicity of cigarette smoke.

BPA and Male Sexual Dysunction

Bisphenol A (BPA) is used in a large number of consumer products, including plastic containers and food and beverage can linings. Following up on an earlier study[4] comparing workers with and without occupational BPA exposure, researchers assessed urine BPA levels and sexual function in a subset of workers and found that increasing urine BPA level was associated with decreasing values for seven measures of sexual function.[5] An additional analysis restricted to workers exposed to BPA only nonoccupationally revealed a similar trend, but the authors wrote that "many of the estimates were no longer statistically significant due to the markedly reduced sample size."

Indoor Tanning and Melanoma: Evidence Strengthens

A new study presents strong evidence that use of tanning beds may lead to higher odds of melanoma.[6] Compared with people who never tanned indoors, people using any tanning bed were almost 75% more likely to develop melanoma, and frequent users of indoor tanning beds had the highest risk. The study also showed for the first time that melanoma was more strongly associated with frequency of tanning than with age at which indoor tanning began. Earlier studies showed only weak associations with melanoma risk; most were unable to adjust for sun exposure or did not confirm dose response or compare specific tanning devices—gaps bridged in the current population-based case–control study. Melanoma, the most dangerous form of skin cancer, is also one of the fastest increasing cancers in the United States.[7]

An advisory panel to the FDA has recommended restrictions on the use of tanning beds by teenagers.

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